REMARKS

Following this response, claims 27-36 and 47-50 are pending in this application. Claims 1-26, 37-26, and 51 have been withdrawn by the Examiner. Claims 27-36 and 47-50 presently stand rejected. Claim 27 is presently amended. Applicants also submit herewith a Declaration of Gilbert R. Gonzales under 37 C.F.R. 1.132 ("Declaration"). In view of these amendments, the Declaration, and the discussion below, it is submitted that the application is now in condition for allowance.

Claim Rejections 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 27-36 and 47-50 (including independent claims 27 and 47) under 35 U.S.C. 112, first paragraph as lacking written description. In a previous response (dated May 28, 2008), Applicants amended independent claims 27 and 47 to recite "a gas-dispersing component including a solid matrix having at least one interior space with at least one first gas contained therein," (with the phrase "at least one interior space with" being added). In the present Office Action, the Examiner states that the specification does not support this amendment because the "at least one interior space" is not recited in the specification, and that no support for the phrase is apparent from the specification. Applicant respectfully disagrees.

Applicant submits that at least paragraph [0024] of the specification provides support for "at least one interior space." In pertinent part, that paragraph

states:

> "Suitable gas-dispersing components may be produced by dispersing the gas within a liquid, molten sugar, or other suitably dispersing liquid or medium, and then solidifying the dispersing medium *to form a bubble, which contains or 'entraps' the gas therein*. The resulting gas-dispersing component is generally referred to as a 'solid foam' (emphasis added)."

Applicant submits that a "bubble" that "entraps the gas therein" does provide support for the recitation of a matrix having "at least one interior space with at least one first gas contained therein," as recited by independent claims 27 and 47. As is well known to those of ordinary skill in the art, a "bubble" inherently includes an interior space. Indeed, the very fact that the specification recites that the bubble entraps the gas therein would require that there be an interior space. Finally, one common definition of a bubble is "a pocket formed in a solid by trapped air or gas, as during cooling" (see The American Heritage Dictionary, 3rd ed., 1997, p. 181).

In view of the above, Applicant respectfully requests a withdrawal of the rejection of independent claims 27 and 47 under 35 U.S.C. 112, first paragraph. And, as claims 28-36 and 48-50 each depend ultimately from either independent claim 27 or independent claim 47, Applicant respectfully requests withdrawal of the rejection of claims 28-36 and 48-50 under 35 U.S.C. 112, first paragraph.

Claim Rejections 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 27-36 and 47-50 (including independent claims 27 and 47) under 35 U.S.C. 112, second paragraph, as being indefinite. In particular, the Examiner states that the term "at least about" is not defined by the claim, the specification does not provide a standard for the term, and one of ordinary skill in the art would not be reasonably apprised of the scope. In response, Applicant has presently amended independent claims 27 and 47 such that the term "at least about" no longer appears in the claims. In view of these amendments, Applicant respectfully requests a withdrawal of the rejection of independent claims 27 and 47 under 35 U.S.C. 112, second paragraph. And, as claims 28-36 and 48-50 each depend ultimately from either independent claim 27 or independent claim 47, Applicant respectfully requests withdrawal of the rejection of claims 28-36 and 48-50 under 35 U.S.C. 112, second paragraph.

Claim Rejections 35 U.S.C. § 102(b)

The Examiner has rejected claims 27, 32-36, and 47-50 under 35 U.S.C. 102(b) as anticipated by U.S. Patent No. 4,687,662 (Schobel). In particular, the Examiner points to column 3, lines 10-12, and the abstract of Schobel, and states that Schobel discloses a method for oral administration of an effervescent composition in the form of tablets or powders including a therapeutic agent, a granulating agent, a microparticulate effervescent component and an effervescent system that dissolve

rapidly in water to yield an effervescent solution containing a completely dissolved therapeutic agent. The Examiner further states that the granulating agent of Schobel causes slow disintegration of the therapeutic agent and release of gas (citing column 4, lines 17-28), and that the effervescent system includes compounds capable of reacting with carbonate containing materials to cause the release of carbon dioxide when contacted with sufficient water (citing column 5, lines 14-18 and lines 45 et seq.). Applicant respectfully disagrees with the rejection under 35 U.S.C. § 102(b).

In particular, Applicant submits that Schobel does not teach any "matrix having at least one interior space with at least one first gas contained therein," as recited in the presently pending claims. As described at column 2, lines 20-27 of Schobel, the composition of that reference includes (1) a preblended mixture of (a) a granulated therapeutic agent and (b) a component of an effervescent system; and (2) other components of the effervescent system. In the preblended mixture, the granulated therapeutic agent and the component of the effervescent system (which is described in Schobel as being a "microparticulate acid") are of roughly similar size (the granulated therapeutic agent being between 100-600 microns and the microparticulate acid being 50-600 microns).

The "microparticulate acids," described in Schobel, are capable of reacting with carbonate-containing materials to cause the release of carbon dioxide when contacted with a sufficient amount of water. As described above, in Schobel, a

granulated therapeutic agent (of 100-600 microns) and microparticulate acids (of 50-600 microns) are admixed to form a preblended mixture. The microparticulate acids are one component of the effervescent system. The remainder of the effervescent system includes all the ingredients of a rapid-dissolving effervescent composition, except for the microparticulate acids as stated at column 5, lines 43-45. And in particular, at column 5, lines 45-64, Schobel describes that the remainder of that effervescent system uses carbonate-containing materials. The various components of the Schobel composition (the preblended mixture of therapeutic agent and microparticulate acid, and the carbonate-containing materials of the remainder of the effervescent system) can then be formed into a desirable shape, such as a tablet, to render a final product.

In use, this tablet is added to an aqueous environment (such as water), causing the microparticulate acids to react with the carbonate-containing materials to release carbon dioxide. Thus, the discussion of a "gas" in Schobel is directed to this generation of carbon dioxide. Nowhere does Schobel describe a gas that is already disposed within an interior compartment (such as being entrapped within a bubble). Applicants thus submit that Schobel does not disclose a solid ingestible pharmaceutical composition including "a gas-dispersing component including a solid matrix having at least one interior space with at least one first gas contained therein," as is recited in independent claims 27 and 47 of the present application.

In view of the above, Applicants respectfully request a withdrawal of the rejection of claims 27 and 47 as anticipated by Schobel. Further, as each of claims 32-36 and 48-50 ultimately depend from either independent claim 27 or independent claim 47, Applicants respectfully request a withdrawal of the rejection of claims 32-36 and 48-50 as anticipated by Schobel.

Claim Rejections 35 U.S.C. § 103

Further, the Examiner has rejected claims 27-36 and 47-50 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,071,539 (Robinson) in view of U.S. Patent No. 3,012,893 (Kremzner). In particular, the Examiner states that Robinson generally teaches effervescent granules having a controllable rate of effervescence, and that Robinson only fails to teach a gas dispersing component included in a solid matrix. For this limitation, the Examiner then points to Kremzner, stating that Kremzner teaches a method of enclosing a gas within a solid matrix, and so provides a gas dispersing component included in a solid matrix. The Examiner suggests that one of ordinary skill in the art would combine the teachings of Robinson and Kremzner to reach the presently claimed invention. Applicants respectfully disagree.

The present application describes and claims a formulation that includes (1) a gas dispersing component, (2) a gas-generating effervescent component, and (3) a medicament. The formulation is placed in an aqueous vehicle, such as an aqueous

food or beverage, containing a minimal amount of water, such as at least 0.1 ml of water. Upon contact with even a minimal amount of water, the dispersing component releases at least one first gas, and the gas-generating effervescent component reacts to produce at least one second gas, both of which are released into the vehicle. As the formulation breaks down in the vehicle, the medicament is also released, and the released first gas disperses the effervescence of the second gas to enhance distribution and dispersion of the medicament within the vehicle. The effervescing second gas enhances penetration of the medicament in the vehicle. The vehicle is then administered to the patient. This method of administering the medicament is particularly useful in pediatric and ostomy patients, for example, cancer patients with gastrostomies, ileostomies, jejunostomies, and colostomies. The method provides for local delivery and dispersion of medicament, which is of great need in these patients, and has not previously been effectively provided. (See also Declaration, paragraph [0008]).

Prior to the present claimed invention, many pharmaceutical formulations containing effervescent components have been proposed to enhance ingestion and/or absorption of active pharmaceutical ingredients. Many of these are listed in the Background section of the present application. And, Robinson itself describes a composition which only includes effervescent granules. However, all of these prior formulations only include effervescent components. Unlike the invention of the present application, none of them also include a gas-dispersing component to assist in the

dispersal of the effervescent component and the medicament. (See also Declaration, paragraph [0009]).

And Applicants note that this distinction is present in both pending independent claims. Independent claims 27 and 47 each recite a "pharmaceutical composition" comprising a "medicament," along with the gas-dispersing component and the gas-generating effervescent component. Thus, the gas-dispersing component and gas-generating effervescent component are used to disperse and distribute a medication in a vehicle to be administered to a patient in need. Thus, the claimed invention of the present application provides, for the first time, effervescence combined with "explosion" (provided by the gas dispersing component) to disperse a medicament, and which can operate in a substance having a minimal amount of water. (See also Declaration, paragraph [0010]).

The Examiner argues that this invention is obvious because Robinson teaches effervescent granules, and Kremzner teaches preparing a gas-containing solid matrix. The Examiner suggests that it would have been obvious to combine Kremzner into Robinson because (1) like Kremzner, the formulation of Robinson is also water or saliva activated, and (2) combination of Robinson's effervescent granules with Kremzner's gas-fused fusible sugar composition could provide effective taste-masking.

However, simply because two compositions can both be placed in an aqueous vehicle (water or saliva) does not mean the two compositions should or would

be combined. Gas-fused fusible sugar compositions, such as in Kremzner, (a confection commonly referred to as "pop rocks" or "popping rocks"), have never been used with a medication. Indeed, there is good reason why such compositions have never been used in such a manner. Primarily, prior to the present application, one of ordinary skill in the art would not use popping rocks as a gas-dispersing component to distribute medication because the process of fusion under compression that is described in Kremzner results in a formulation in which the medicament could lack stability. And, when providing a formulation for the delivery of a medicament, the FDA will require formulation specifications to show stability and that denaturation is not taking place. As such, one skilled in the art has never combined compositions such a those of Robinson and Kremzner. It is only the work described in the present application, which goes against the conventional wisdom of those of ordinary skill in the art, that now, for the first time, provides such a combination. (See also Declaration, paragraph [0012]).

Further, nowhere does Kremzner suggest that his composition can be used to disperse medications (nor would it, since one skilled in the art would not have used such a composition with a medicament). The only uses for the composition described in Kremzner are as a vehicle for gas storage, a carbonating agent in beverages, a leavening agent in baking, and as a carbonated hard candy (see column 3, lines 55-68). None of these uses are even remotely similar to a use to disperse a medication or medications. And nowhere does Kremzner mention any medicament as

a potential ingredient of the formulation. Apart from the sugars and gas used to form the fusible sugar/gas composition, Kremzner only mentions edible acids, buffer salts, flavors, and coloring as other materials that may be added (see column 2, lines 63-70). Since one of ordinary skill in the art would not use the composition of Kremzner with a medicament, Applicants submit that one would not combine the composition of Kremzner with that of Robinson. (See also Declaration, paragraph [0013]).

Further, independent claims 27 and 47 generally recite that the gas is adapted to be released when the composition is combined with as little as 0.1 ml of water (as those claims teach that the aqueous vehicle can include 0.1 ml of water, but regardless the gases will disperse and be generated if there is even only 0.1 ml of water). Applicants submit that one of ordinary skill in the art also would not think that subjecting the composition of Kremzner to an oligohydrous condition (i.e. a minimal water environment like apple sauce) would lead to explosion and effervescence ("explosion" referring to the release of compressed gas in popping rocks). To that end, Kremzner states that its composition can dissolve in water, but never lists any amounts of water. However, Kremzner does describe that the compositions may be used for carbonating beverages, and as hard candies. A beverage would include more than 0.1 ml of water, and a hard candy would dissolve in the mouth as a result of contact with the saliva (as described by Kremzner) – which would be present in more than 0.1 ml. Thus, Kremzner does not describe a composition that will "explode" in an oligohydrous

condition including as little as 0.1 ml water. Nor does Robinson suggest an oligohydrous condition when using its composition. Thus, Applicants submit that it would not be obvious to combine the compositions of Robinson and Kremzner for use in an oligohydrous condition. (See also Declaration, paragraph [0014]).

In view of the above, Applicants submit that claims 27-36 and 47-50 are not rendered obvious by Robinson in view of Kremzner, and respectfully request a withdrawal of the rejection of same.

Conclusion

For the foregoing reasons, it is submitted that all claims are patentable, and a Notice of Allowance is respectfully requested.

Please consider this paper a Petition of Extension of Time of two months. The Commissioner is authorized to charge Deposit Account No. 23-3000 in the amount of $245.00 for a two month extension under 37 C.F.R. 1.17(a)(2). Any deficiencies or credits necessary to complete this communication should be applied to Deposit Account No. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,
WOOD, HERRON & EVANS, L.L.P.

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